REMARKS

Status of the Application

Claims 31-39 are under current consideration, and stand rejected. Claim 38 has been amended. Claims 31-39 remain pending in the instant application.

The amendments to the claims do not add or constitute new matter. Support for the amendments to the claims may be found throughout the specification. Specifically, support for the amendment to claim 38 regarding use of mouse embryonic stem cells can be found at, for example, page 12, line 25 through page 13, line 14, of the specification. As such, no new matter has been added by this amendment.

The foregoing amendments are made solely to expedite prosecution of the instant application, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. Applicants reserve the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Applicants respectfully request reconsideration of the application in view of the amendments to the claims, and remarks made herein.

Rejection under 35 U.S.C. § 101

The Examiner has rejected claims 31-39 under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either a specific or substantial asserted utility or a well-established utility. Applicants respectfully traverse the rejection. However, Applicants submit that the rejection has been overcome in light of the arguments below.

Specifically, the Examiner has stated that the asserted utility for the claimed transgenic mice does not appear to be specific and substantial. The Examiner has based the rejection on the evidence of record allegedly not providing a correlation between the phenotypes exhibited by the claimed mice and any disease or disorder. The Examiner further asserts that the evidence of record has failed to provide a correlation between any chemokine receptor 9A related disease or disorder and the phenotypes exhibited by the claimed mouse. Applicants respectfully disagree. However, although Applicants submit that the correlation has been provided, and is well-established in the art, Applicants do not believe that the assertion of such a correlation is necessary for the establishment of utility and for the patentability of the claimed transgenic mouse. For the

reasons set forth below, Applicants submit that the Examiner's rejection of the claims for lack of utility is improper.

Claims 31-39 and are drawn to a transgenic mouse whose genome comprises a disruption in the endogenous chemokine receptor 9A gene, wherein the mouse exhibits decreased agility, coordination or balance, and to a method of making said transgenic mouse. Applicants have asserted in the specification several potential uses for the transgenic knockout mouse, and such uses of transgenic knockout mice are well accepted within the art. See, for example, page 5, lines 12-19, page 6, lines 5-14, page 18, line 16 through page 19, line 19, page 19, lines 25-30 and page 20, lines 1-5, of the specification. The potential uses specifically relate to using the mice to discover, examine and/or develop potential treatments, which may include therapeutic agents, capable of modulating the phenotype exhibited by the mice, and in particular, capable of modulating or ameliorating the decreased or impaired agility, coordination or balance exhibited by the mice. Although Applicants have suggested these potential uses for the transgenic mice, many well-established uses for the mice would be recognized by a person skilled in the art.

Applicants submit that in order to satisfy the utility requirements set forth in 35 U.S.C. § 101, the specification must assert a specific and substantial utility that is credible to a skilled artisan, or the utility of the claimed invention must be apparent to the skilled artisan. See MPEP § 2107. Applicants submit that the instant specification satisfies these requirements.

The instant specification has demonstrated that disruption of the chemokine receptor 9A sequence as described in SEQ ID NO:1 in a mouse results in a phenotype specific to that mouse. In particular, the transgenic mice whose genomes comprise this disruption exhibit impaired agility, coordination and balance when compared to wild-type mice, which was characterized by a decreased performance on an accelerating rotarod (See page 5, lines 15-20 of the specification, and Table 1). The phenotypic parameters of the transgenic mice were evaluated in controlled studies, which are well-established as tests locomotor coordination, agility and balance.

It is generally accepted in the art that transgenic knockout mice, such as those described in and claimed by the instant application, represent a valuable tool for determining the function of genes in various conditions or disorders. It is also generally accepted that gene function is related to and representative of that of human, in light of the homology between the mouse and human genomes. This is why knockout mice represent such a valuable tool. In the present case, the transgenic mouse described in the instant specification would be accepted by the skilled artisan as

a model for the role and function of the chemokine receptor 9A gene. Applicants' disclosure related to the phenotype of the transgenic mice has established that this gene plays a role in agility, coordination and balance, as noted above. More particularly, loss of function of the chemokine receptor 9A gene and/or protein has been demonstrated to have detrimental effects on agility, coordination and/or balance in the knockout mice. The value of such an *in vivo* model of chemokine receptor 9A gene function would be immediately recognized by a person skilled in the art. This is supported by the trend to produce such transgenic mice with disruptions in virtually every gene.

The Examiner has stated that no correlation has been established between the decreased agility, coordination and balance phenotype and any disease or disorder. As noted above, Applicants do not believe that this is a requirement in order to establish that the transgenic mice have utility. However, despite Applicants' belief that no such requirement exists, Applicants submit that a correlation does exist. In particular, a relationship exists between the phenotype exhibited by the transgenic mice and conditions or disorders related to agility, coordination and balance, which would be recognized within the art. Applicants submit that a desire exists to ameliorate such conditions as impaired balance, agility or coordination associated with motor function related disorders or conditions, including but not limited to Parkinson's disease or Huntington's disease. Applicants also submit that the skilled artisan would recognize that the motor impaired mice as claimed could also be used as a tool for investigating methods for improving motor function, coordination, balance and/or agility. As such, the claimed mice clearly have well-established, real world uses that would be evident to the skilled artisan.

The Examiner has cited Crabbe (*Science*, 1999, Vol. 284, pp 1670-1672) as establishing that results obtained from behavioral studies are greatly influenced by the genetic background of the tested mouse. However, the Crabbe reference fails to establish that phenotypic differences between a transgenic knockout mouse and a wild-type control mouse, such as those described in the instant specification, are not real and a result of the disruption of the target gene. In particular, the Crabbe reference compares only one null mutant strain (for the 5-HT1B gene) to inbred wild-type strains, and is not representative of a comparison of all mutant knockout mice and their wild-type control counterparts. Further, the number of mice tested was low, and, even according to the reference, "made formal statistical assessment of reliability infeasible" (see page 1671, column 3,

first full paragraph). The Crabbe reference also states that the results obtained in their study can be interpreted in different ways.

Despite Applicants' belief that the Crabbe reference should not be broadly interpreted to apply to all behavioral mouse studies, Crabbe only describes the open field test, the elevated plus maze, and the water maze test, and fails to describe all behavioral tests. More particularly, Crabbe fails to describe any problems in consistency between labs demonstrated for the rotarod test as used by Applicants. The rotarod test is a classic method for the evaluation of locomotor coordination used by many people skilled in the art to test mice, including knockout mice. Furthermore, the rotarod test described in the instant specification compares the homozygous knockout mice to wild-type age- and gender-matched wild-type mice in a controlled laboratory setting. The results would be accepted by the skilled artisan as demonstrating a role for the chemokine receptor 9A in coordination, balance and/or agility. As such, Applicants submit that the Crabbe reference fails to establish that the claimed mice lack utility.

Applicants submit that they have demonstrated in the arguments above and in the originally filed specification that a correlation between the phenotype exhibited by the claimed mice, the chemokine receptor 9A gene and motor related disorders are well-established and described in the specification. However, even in the absence of this correlation, the transgenic mice have been asserted and demonstrated as useful for discovering treatments, including therapeutic agents, capable of modulating a phenotype exhibited by the mice. As noted above, Applicants are not aware of any requirement for a correlation between a phenotype and a specific disease in order to establish the utility of a transgenic mouse. Applicants submit that the utility of a transgenic knockout mouse such as that claimed herein would be immediately apparent to the skilled artisan.

In summary, Applicants have asserted in the specification several specific and substantial uses for the claimed transgenic mice. Further, in light of the art-recognized value of and demand for transgenic knockout mice, the asserted utilities are among many that are well-established and credible to the skilled artisan.

In view the arguments set forth above, Applicants believe the rejection of the claims under 35 U.S.C. § 101 is improper, and respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 31-39 under 35 U.S.C. § 112, first paragraph, because one skilled in the art would allegedly not know how to use the claimed invention as a result of the alleged lack of either a specific or substantial asserted utility or a well-established utility for the reasons set forth in the utility rejection. Applicants respectfully traverse the rejection. However, for the reasons set forth above in response to the utility rejection, Applicants submit that the rejection under 35 U.S.C. § 112, first paragraph, is improper. Therefore, Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 38 and 39 under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse the rejection.

Specifically, the Examiner has asserted that the term "murine" in claim 38 renders the claim indefinite because it is unclear how a transgenic mouse can be produced when using a rat embryonic stem cell, which the Examiner alleges is encompassed by the term. The Examiner has indicated that amending the claim to read on a mouse embryonic stem cell will obviate this rejection. Applicants have adopted this suggestion, and the claims now recite a mouse embryonic stem cell. Claim 39 depends from claim 38. In light of Applicants' amendment, the rejection under 35 U.S.C. § 112, second paragraph, has been overcome, and Applicants respectfully request withdrawal of the rejection.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-365.

Respectfully submitted,

Date: April 5, 2004

Kelly L. Quast

Kelly L. Quast, Reg. No. 52,141

Deltagen, Inc.
1031 Bing Street
San Carlos, CA 94070
(650) 569-5100